

Application No.: 09/689,281 Inventor: Stephen C. Cosenza, et al.

fee is believed due in connection with the filing of this paper. Submitted herewith is (a) Exhibit A, a market up version of claims showing the amendments made therein; (b) Exhibit B, a copy of the claims pending upon entry of the amendment; (c) Exhibit (C), an entry for amifostine from The Merck Index 12th Edit., Merck & Co., Inc., Whitehouse Station, NJ (1996); and (d) Exhibit D, a copy of an abstract entitled "Cytoprotectant Amifostine Approved".

It is not believed that extensions of time or fees are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional fees are necessary to prevent abandonment of this application, then such fees are hereby authorized to be charged to Drinker Biddle & Reath LLP Deposit Account No. 50-0573.

AMENDMENTS

IN THE CLAIMS:

Attached herewith is Exhibit A, a marked up version of the claims showing the amendments made herein.

Please cancel Claims 13, 16, and 19, without prejudice.

Please re write Claims 1, 14, 17, 18, and 20 as follows:



1. (Twice Amended) A method for protecting an animal from cytotoxic side effects of the administration of a mitotic phase cell cycle inhibitor or a topoisomerase inhibitor comprising administering to the animal, at least about 4 hours before administration of the inhibitor an effective amount of at least one cytoprotective α, β unsaturated aryl sulfone compound, wherein the mitotic phase cell cycle inhibitor is selected from the group consisting of vinca alkaloids, taxanes, naturally occurring macrolides, and colchicine and its derivatives and the topoisomerase inhibitor is selected from the group consisting of camptothecin, etoposide and mitoxantrone.

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14. (Once Amended) The method according to claim 1 wherein the cytoprotective compound is administered at least about 12 hours before administration of the mitotic phase cell cycle inhibitor or topoisomerase inhibitor.



17. (Once Amended) The method according to claim 1 wherein the mitotic phase cell cycle inhibitor is selected from the group consisting of paclitaxel and vincristine.



18. (Thrice Amended) In a method for treating cancer or other proliferative disorder comprising administering an effective amount of at least one mitotic phase cell cycle inhibitor or topoisomerase inhibitor to an animal in need of such treatment, the improvement comprising administering to the animal at least about 4 hours prior to administration of the mitotic phase cell cycle inhibitor or topoisomerase inhibitor an effective amount at least one cytoprotective α , β unsaturated aryl sulfone compound, wherein the mitotic phase cell cycle inhibitor is selected from the group consisting of vinca alkaloids, taxanes, naturally occurring macrolides, and colchicine and its derivatives and the topoisomerase inhibitor is selected from the group consisting of camptothecin, etoposide and mitoxantrone, and wherein the animal is protected from the cytotoxic side effects of the administration of the mitotic phase cell cycle inhibitor or topoisomerase inhibitor.



20. (Once Amended) The method according to claim 18 wherein the cytoprotective compound is administered at least about 12 hours before administration of the mitotic phase cell cycle inhibitor or topoisomerase inhibitor.

Please add the new claims 23-28.



23. (New) The method according to claim 1 wherein the cytoprotective compound is according to formula VI:

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$$R_1$$
 R_2 R_3 R_4 R_4

wherein:

R₁, R₂, R₃ and R₄ are independently selected from the group consisting of hydrogen, halogen, C1-C8 alkyl, C1-C8 alkoxy, nitro, cyano, carboxy, hydroxy and trifluoromethyl; or a pharmaceutically acceptable salt thereof.

24. (New) The method according to claim 1 wherein the cytoprotective compound is according to formula VII:

$$\begin{array}{c|c} Q_3 & O \\ & \parallel & \vee \parallel \\ HC & C \\ & Q_5 \\ & Q_2 \\ & Q_4 \end{array}$$

Wherein

 Q_3 , Q_4 and Q_5 are independently selected from the group consisting of phenyl and mono-, di-, tri-, tetra- and penta-substituted phenyl where the substituents, which may be the same or different, are independently selected from the group consisting of halogen, C1-C8 alkyl, C1-C8 alkoxy, nitro, cyano, carboxy, hydroxy, phosphonato, amino, sulfamyl, acetoxy,

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dimethylamino(C2-C6 alkoxy), C1-C6 trifluoroalkoxy and trifluoromethyl; or a pharmaceutically acceptable salt thereof.

25. (New) The method according to claim 24 wherein the cytoprotective compound is according to formula VIIa:



wherein

 R_1 and R_2 are independently selected from the group consisting of hydrogen, halogen, C1-C8 alkyl, C1-8 alkoxy, nitro, cyano, carboxy, hydroxy, and trifluoromethyl; and

R₃ is selected from the group consisting of unsubstituted phenyl, mono-substituted phenyl and di-substituted phenyl, the substituents on the phenyl ring being independently selected from the group consisting of halogen and C1-8 alkyl; or a pharmaceutically acceptable salt thereof.

- 26. (New) The method of claim 25 wherein the cytoprotective compound is 2-(phenylsulfonyl)-1-phenyl-3-(4-fluorophenyl)-2-propen-1-one.
 - 27. (New) The method according to claim 1, wherein the animal is a human being.
 - 28. (New) The method according to claim 18, wherein the animal is a human being.